

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	26	"indoleamine-2,3-dioxygenase"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 10:43
L2	28616	"indoleamine-2,3-dioxygenase" or "IDO" or (indoleamine 2, 3-dioxygenase)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 10:43
L3	28271	"indoleamine-2,3-dioxygenase" or "IDO" or ("indoleamine 2, 3-dioxygenase")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 10:43
L4	142	"indoleamine-2,3-dioxygenase" or ("indoleamine 2,3-dioxygenase")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 10:55
L5	24	("indoleamine-2,3-dioxygenase" or "indoleamine 2,3-dioxygenase").clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 10:46
L6	4	("1-MT" or "1-methyl-tryptophan"). clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 10:46
L7	7	"indoleamine-2,3-dioxygenase inhibitor" or ("indoleamine 2, 3-dioxygenase inhibitor")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 10:47
L8	0	("indoleamine-2,3-dioxygenase" or "indoleamine 2,3-dioxygenase") near cancer	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 10:55

## EAST Search History

L9	3	("indoleamine-2,3-dioxygenase" or "indoleamine 2,3-dioxygenase") near tumor	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 10:55
L10	30	("indoleamine-2,3-dioxygenase" or "indoleamine 2,3-dioxygenase") same tumor	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 15:35
L11	43	("indoleamine-2,3-dioxygenase" or "indoleamine 2,3-dioxygenase") same cancer	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 13:17
L12	2	"20010044457"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 13:18
L13	1932	514/419	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 15:35
L14	1577	514/419.ccls.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 15:36
L15	6	l14 and l1	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/03/22 15:36

FILE 'HOME' ENTERED AT 11:18:22 ON 22 MAR 2007

=> file medline caplus wpids

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'MEDLINE' ENTERED AT 11:18:48 ON 22 MAR 2007

FILE 'CAPLUS' ENTERED AT 11:18:48 ON 22 MAR 2007

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FILE 'WPIDS' ENTERED AT 11:18:48 ON 22 MAR 2007

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=> s "1-methyl-tryptophan"

L1 64 "1-METHYL-TRYPTOPHAN"

=> s l1 and cancer

L2 13 L1 AND CANCER

=> s l1 and ("cancer" or "tumor")

L3 24 L1 AND ("CANCER" OR "TUMOR")

=> s l3 not py>2002

L4 4 L3 NOT PY>2002

=> d l4 1-4 ibib, abs, hitstr

L4 ANSWER 1 OF 4 MEDLINE on STN

ACCESSION NUMBER: 2002453562 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12209992

TITLE: Indoleamine 2,3-dioxygenase contributes to tumor cell evasion of T cell-mediated rejection.

AUTHOR: Friberg Maria; Jennings Ronald; Alsarraj Marwan; Dessureault Sophie; Cantor Alan; Extermann Martine; Mellor Andrew L; Munn David H; Antonia Scott J

CORPORATE SOURCE: Department of Interdisciplinary Oncology, H. Lee Moffitt Cancer Center, Tampa, FL 33612, USA.

SOURCE: International journal of cancer. Journal international du cancer, (2002 Sep 10) Vol. 101, No. 2, pp. 151-5. Journal code: 0042124. ISSN: 0020-7136.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200210

ENTRY DATE: Entered STN: 6 Sep 2002

Last Updated on STN: 2 Oct 2002

Entered Medline: 1 Oct 2002

AB The priming of an appropriate anti-tumor T cell response rarely results in the rejection of established tumors. The characteristics of tumors that allow them to evade a T cell-mediated rejection are unknown for many tumors. We report on evidence that the expression of the immunosuppressive enzyme, indoleamine 2,3-dioxygenase (IDO) by mononuclear cells that invade tumors and tumor-draining lymph nodes, is 1 mechanism that may account for this observation. Lewis lung carcinoma (LLC) cells stimulated a more robust allogeneic T cell response in vitro in the presence of a competitive inhibitor

of IDO, 1- methyl tryptophan. When administered in vivo this inhibitor also resulted in delayed LLC tumor growth in syngeneic mice. Our study provides evidence for a novel mechanism whereby tumors evade rejection by the immune system, and suggests the possibility that inhibiting IDO may be developed as an anti-cancer immunotherapeutic strategy.  
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L4 ANSWER 2 OF 4 WPIDS COPYRIGHT 2007 THE THOMSON CORP on STN  
ACCESSION NUMBER: 2003-119014 [11] WPIDS  
CROSS REFERENCE: 1999-394927; 1999-394973; 2002-546166; 2002-546465;  
2003-227919; 2003-228111  
DOC. NO. CPI: C2003-030680 [11]  
TITLE: Increasing T cell activation by an antigen-bearing cell  
for altering maternal tolerance of pregnancy, by  
administering to a subject a pharmaceutical composition  
comprising indoleamine-2,3-dioxygenase inhibitor  
DERWENT CLASS: B02  
INVENTOR: MELLOR A; MUNN D  
PATENT ASSIGNEE: (MEDI-N) MEDICAL COLLEGE GEORGIA RES INST  
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 6451840	B1	20020917	(200311)*	EN	27	[11]

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6451840	B1 Provisional	US 1997-67610P	19971205
US 6451840	B1 Provisional	US 1998-80380P	19980401
US 6451840	B1 Provisional	US 1998-80384P	19980401
US 6451840	B1	US 1998-206274	19981204

PRIORITY APPLN. INFO: US 1998-206274 19981204  
US 1997-67610P 19971205  
US 1998-80380P 19980401  
US 1998-80384P 19980401

AN 2003-119014 [11] WPIDS  
CR 1999-394927; 1999-394973; 2002-546166; 2002-546465; 2003-227919;  
2003-228111  
AB US 6451840 B1 UPAB: 20050528

NOVELTY - Increasing (M) T cell activation by an antigen-bearing cell, involves administering an amount of a pharmaceutical composition (I) comprising an inhibitor of indoleamine-2,3-dioxygenase.

ACTIVITY - Anti-HIV; Antiinflammatory; Cytostatic.

Inhibition of tumor growth by administration of indoleamine-2,3-dioxygenase (IDO) inhibitor was as follows. Tumor -bearing hosts were treated with the IDO inhibitor 1- methyl-tryptophan. MB49 tumor cells (1x10<sup>6</sup>) were injected subcutaneously into syngeneic C57/B16 host. Pellets containing 1- methyl-tryptophan (0.9 mg/hour, 7-day release) were implanted at the time of tumor cell inoculation. By day 10, all animals had evidence of initial tumor formation (palpable mass). By day 15, control animals were visibly ill and the experiment was terminated. Animals were sacrificed on day 11-15 for histologic examination. The results showed that, administration of 1-methyl-tryptophan significantly reduced tumor growth in immunocompetent, syngeneic hosts, compared to vehicle control.

MECHANISM OF ACTION - Inhibitor of indoleamine-2,3-dioxygenase (claimed); Enhancer of T cell activation; Inducer of rejection of a fetus; Inhibitor of tumor growth.

USE - (M) is useful for increasing T cell activation by an antigen-bearing cell in a subject, preferably human (claimed). (M) is useful to enhance T cell activation when the T cells are suppressed by pregnancy, malignancy or a virus such as human immunodeficiency virus (HIV). (M) is useful for altering maternal tolerance of pregnancy, to affect infection by certain viruses such as HIV and inflammation, to induce rejection of a fetus, to terminate or prevent pregnancy, or to inhibit tumor growth.

=> FIL STNGUIDE

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

28.51

28.72

FILE 'STNGUIDE' ENTERED AT 11:21:19 ON 22 MAR 2007

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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Mar 16, 2007 (20070316/UP).

=> file medline caplus wpids

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.06

28.78

FILE 'MEDLINE' ENTERED AT 11:22:01 ON 22 MAR 2007

FILE 'CAPLUS' ENTERED AT 11:22:01 ON 22 MAR 2007

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FILE 'WPIDS' ENTERED AT 11:22:01 ON 22 MAR 2007

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=> s "indoleamine 2,3-dioxygenase"

L5 1454 "INDOLEAMINE 2,3-DIOXYGENASE"

=> s 15 and cancer

L6 136 L5 AND CANCER

=> s 16 and inhibitor

L7 34 L6 AND INHIBITOR

=> s 17 not py>2002

L8 4 L7 NOT PY>2002

=> d 18 1-4 ibib abs

L8 ANSWER 1 OF 4 MEDLINE on STN

ACCESSION NUMBER: 2002453562 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12209992

TITLE: Indoleamine 2,3-

dioxygenase contributes to tumor cell evasion of T cell-mediated rejection.

AUTHOR: Friberg Maria; Jennings Ronald; Alsarraj Marwan; Dessureault Sophie; Cantor Alan; Extermann Martine; Mellor Andrew L; Munn David H; Antonia Scott J  
CORPORATE SOURCE: Department of Interdisciplinary Oncology, H. Lee Moffitt Cancer Center, Tampa, FL 33612, USA.  
SOURCE: International journal of cancer. Journal international du cancer, (2002 Sep 10) Vol. 101, No. 2, pp. 151-5.  
Journal code: 0042124. ISSN: 0020-7136.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200210  
ENTRY DATE: Entered STN: 6 Sep 2002  
Last Updated on STN: 2 Oct 2002  
Entered Medline: 1 Oct 2002

AB The priming of an appropriate anti-tumor T cell response rarely results in the rejection of established tumors. The characteristics of tumors that allow them to evade a T cell-mediated rejection are unknown for many tumors. We report on evidence that the expression of the immunosuppressive enzyme, indoleamine 2,3- dioxygenase (IDO) by mononuclear cells that invade tumors and tumor-draining lymph nodes, is 1 mechanism that may account for this observation. Lewis lung carcinoma (LLC) cells stimulated a more robust allogeneic T cell response in vitro in the presence of a competitive inhibitor of IDO, 1-methyl tryptophan. When administered in vivo this inhibitor also resulted in delayed LLC tumor growth in syngeneic mice. Our study provides evidence for a novel mechanism whereby tumors evade rejection by the immune system, and suggests the possibility that inhibiting IDO may be developed as an anti-cancer immunotherapeutic strategy.  
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L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2002:674702 CAPLUS Full-text  
DOCUMENT NUMBER: 137:200238  
TITLE: Indoleamine 2,3-

dioxygenase contributes to tumor cell evasion of T cell-mediated rejection  
AUTHOR(S): Friberg, Maria; Jennings, Ronald; Alsarraj, Marwan; Dessureault, Sophie; Cantor, Alan; Extermann, Martine; Mellor, Andrew L.; Munn, David H.; Antonia, Scott J.  
CORPORATE SOURCE: Department of Interdisciplinary Oncology, H. Lee Moffitt Cancer Center, Tampa, FL, 33612, USA  
SOURCE: International Journal of Cancer (2002), 101(2), 151-155  
CODEN: IJCNW; ISSN: 0020-7136  
PUBLISHER: Wiley-Liss, Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The priming of an appropriate antitumor T cell response rarely results in the rejection of established tumors. The characteristics of tumors that allow them to evade a T cell-mediated rejection are unknown for many tumors. The authors report on evidence that the expression of the immunosuppressive enzyme, indoleamine 2,3- dioxygenase (IDO) by mononuclear cells that invade tumors and tumor-draining lymph nodes, is a mechanism that may account for this observation. Lewis lung carcinoma (LLC) cells stimulated a more robust allogeneic T cell response in vitro in the presence of a competitive inhibitor of IDO, I-Me tryptophan. When administered in vivo this inhibitor also

resulted in delayed LLC tumor growth in syngeneic mice. The authors' study provides evidence for a novel mechanism whereby tumors evade rejection by the immune system, and suggests the possibility that inhibiting IDO may be developed as an anti-cancer immunotherapeutic strategy.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:649764 CAPLUS Full-text

DOCUMENT NUMBER: 117:249764

TITLE: Differential induction of indoleamine-2,3-dioxygenase (IDO) by interferon- $\gamma$  in human gynecologic cancer cells

AUTHOR(S): Leung, Benjamin S.; Stout, Lawrence E.; Shaskan, Edward G.; Thompson, Randall M.

CORPORATE SOURCE: Clin. Hosp., Univ. Minnesota, Minneapolis, MN, 55455, USA

SOURCE: Cancer Letters (Shannon, Ireland) (1992), 66(1), 77-81  
CODEN: CALEDQ; ISSN: 0304-3835

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Induction of IDO by interferon- $\gamma$  (IFN- $\gamma$ ) is thought to be a mechanism underlying the antineoplastic properties of IFN- $\gamma$ . Since clin. trials with IFN- $\gamma$  have yielded variable efficacy in treating cancers of gynecol. origin, the effects of IFN- $\gamma$  on cell growth and IDO activity in cell lines from 7 gynecol. and 5 breast cancers were tested. At a dose of 250 IU/mL, IFN- $\gamma$  suppressed cell growth and induced IDO activity in 1 cervical (C41), 1 vulva (A431), 1 breast (HS578T), and 2 ovarian (OVCAR-3, CAOV-3) cancer cell lines. Differing inhibition of cell growth, but with no induction of IDO activity, was found with IFN- $\gamma$  treatment of the other cell lines.

L8 ANSWER 4 OF 4 WPIDS COPYRIGHT 2007 THE THOMSON CORP on STN

ACCESSION NUMBER: 2001-024777 [03] WPIDS

DOC. NO. CPI: C2001-007526 [03]

TITLE: Novel methods for increasing proliferation of cells, especially T cells comprising growing the cells in the presence of tryptophan enhancing agents, useful for treating cancer

DERWENT CLASS: B04; D16

INVENTOR: BILSBOROUGH J; BOON-FALLEUR T; VAN DEN EYNDE B

PATENT ASSIGNEE: (LUDW-N) LUDWIG INST CANCER RES

COUNTRY COUNT: 21

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2000066764	A1	20001109	(200103)*	EN	44 [5]	
AU 2000046976	A	20001117	(200111)	EN		
EP 1185687	A1	20020313	(200225)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000066764	A1	WO 2000-US12118	20000503
AU 2000046976	A	AU 2000-46976	20000503

EP 1185687 A1  
EP 1185687 A1

EP 2000-928796 20000503  
WO 2000-US12118 20000503

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000046976 A	Based on	WO 2000066764 A
EP 1185687 A1	Based on	WO 2000066764 A

PRIORITY APPLN. INFO: US 1999-132219P 19990503

AN 2001-024777 [03] WPIDS

AB WO 2000066764 A1 UPAB: 20050524

NOVELTY - Increasing proliferation of cells (I), comprising growing the cells in the presence of one or more tryptophan enhancing agents, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) determining (II) a condition characterized by the ability of cancer cells to resist or evade T cell-mediated cytotoxicity by monitoring a sample of cancer cells from a patient for constitutive expression of indoleamine 2,3-dioxygenase (IDO);

(2) determining whether to treat a cancer patient with an inhibitor of IDO by determining the constitutive expression of IDO by the cancer cells of the patient, where the constitutive expression of IDO determines that the patient will be treated with an inhibitor of IDO;

(3) treating a subject having or suspected of having a tumor, the cells of which constitutively express IDO by administering an IDO inhibitor effective;

(4) treating a cancer cell which has evaded or has the potential to evade T cell-mediated cytotoxicity by administering a tryptophan enhancing agent to increase T cell-mediated cytotoxicity of the cancer cells;

(5) an apparatus (III) for culturing T cells, comprising a cell culture container containing a tryptophan enhancing agent and at least one T cell;

(6) a kit for stimulating the proliferation of T cells in the absence of cells expressing IDO, comprising a container containing a tryptophan enhancing agent and instructions for using the agent to stimulate proliferation of T cells in vitro in the absence of macrophages and trophoblasts;

(7) a growth medium (IV) for the culture of cells comprising a tryptophan enhancing agent;

(8) a T cell culture comprising at least one T cell, growth medium and a tryptophan enhancing agent; and

(9) an immune response modulation composition (V) comprising a tryptophan enhancing agent effective to increase local tryptophan concentrations in the presence of constitutively expressed IDO.

ACTIVITY - Cytostatic; Immunostimulant.

The effect of the IDO inhibitor, 1-methyl-tryptophan, on inhibiting tumor growth was investigated. Female Balb/c mice (3 groups of 20) were injected subcutaneously with either 100000 or 500000 live cells of the tumor line WEH1 3B which expresses high levels of the T cell inhibitor, IDO. On the day prior to tumor injection and on every second day following tumor injection, the mice underwent therapeutic treatment with an intraperitoneal injection of 10 mg of 1-methyl-tryptophan. Control mice were treated with phosphate buffered saline (PBS). The size of the developing tumor on each mouse was measured every second day. The results showed that treatment with 1-methyl-tryptophan in the group of mice injected with 100000 tumor cells retarded the development of the tumor compared to the rate of growth of tumors in mice treated with PBS. These results suggested that 1-methyl-tryptophan inhibits tumor growth.

MECHANISM OF ACTION - Inhibitor of IDO.



USE - The method is useful for increasing the proliferation of cells,  
especially T cells (claimed). (V) is useful for the treatment of cancer.

=> d his

(FILE 'HOME' ENTERED AT 11:18:22 ON 22 MAR 2007)

FILE 'MEDLINE, CAPLUS, WPIDS' ENTERED AT 11:18:48 ON 22 MAR 2007

L1 64 S "1-METHYL-TRYPTOPHAN"  
L2 13 S L1 AND CANCER  
L3 24 S L1 AND ("CANCER" OR "TUMOR")  
L4 4 S L3 NOT PY>2002

FILE 'STNGUIDE' ENTERED AT 11:21:19 ON 22 MAR 2007

FILE 'MEDLINE, CAPLUS, WPIDS' ENTERED AT 11:22:01 ON 22 MAR 2007

L5 1454 S "INDOLEAMINE 2,3-DIOXYGENASE"  
L6 136 S L5 AND CANCER  
L7 34 S L6 AND INHIBITOR  
L8 4 S L7 NOT PY>2002

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	72.03	100.81
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-1.56	-1.56

STN INTERNATIONAL LOGOFF AT 11:36:31 ON 22 MAR 2007